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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,157	COVACCI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 08/10/04 in response to the non-final Office Action mailed 03/03/04. With this, Applicants have amended the specification.

Status of Claims

2) Claims 38 and 44-46 have been amended via the amendment filed 08/10/04.

Claims 38 and 44-46 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

5) The rejection of claims 38 and 44-46 made or maintained in paragraph 10(d) of the Office Action mailed 10/15/02, paragraph 20 of the Office Action mailed 06/04/03, and maintained in paragraph 7 of the Office Action mailed 03/03/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

6) The rejection of claims 38 and 44-46 made in paragraph 22 of the Office Action mailed 06/04/03 maintained in paragraph 9 of the Office Action mailed 03/03/04 under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendments to the claims. A new or modified rejection is set forth below to meet the limitations in the claims, as amended.

7) The rejection of claims 38 and 44-46 made in paragraph 24 of the Office Action mailed 06/04/03 and made or maintained in paragraph 10 of the Office Action mailed 03/03/04 under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992), is withdrawn in light of Applicants' amendment to the claims. A new or modified rejection is set forth below to meet the limitations in the claims, as amended.

8) The rejection of claims 44 and 46 made in paragraph 25 of the Office Action mailed

06/04/03 and made or maintained in paragraph 11 of the Office Action mailed 03/03/04 under 35 U.S.C. § 102(b) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - Applicants' IDS) (Cover *et al.*, 1992), is withdrawn in light of Applicants' amendment to the claims. A new or modified rejection is set forth below to meet the limitations in the claims, as amended.

9) The rejection of claims 38 and 44-46 made or maintained in paragraph 12 of the Office Action mailed 10/15/02, paragraph 21 of the Office Action mailed 06/04/03 and paragraph 8 of the Office Action mailed 03/03/04 under 35 U.S.C. § 112, first paragraph, as being non-enabled, is withdrawn.

10) The rejection of claims 38 and 45 made in paragraph 13 of the Office Action mailed 03/03/04 under 35 U.S.C. § 102(e) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992 – already of record), is withdrawn in light of Applicants' amendments to the claims. A new/modified rejection is set forth below to reject the claims, as amended.

11) The rejection of claims 38 and 45 made in paragraph 14 of the Office Action mailed 03/03/04 under 35 U.S.C. § 102(b) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 – already of record) (Cover *et al.*, 1992), is withdrawn in light of Applicants' amendments to the claims. A new/modified rejection is set forth below to reject the claims, as amended.

Rejection(s) Maintained

12) The provisional rejection of claims 38 and 44 made in paragraph 9 of the Office Action mailed 10/15/02 and maintained in paragraph 6 of the Office Action mailed 03/03/04 under the judicially created doctrine of obviousness-type double patenting over the cited claims of the co-pending application, 09/360,934, is still maintained for reasons set forth therein. It is noted that Applicants have agreed to submit a terminal disclaimer over SN 09/360,934 upon indication of allowability of the claims.

13) The rejection of claims 45 and 46 made in paragraph 12 of the Office Action mailed 03/03/04 under provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 40, 54, 61-65, 72-75, 82-86, 93 and 94 of the co-pending application, SN 09/360,934, is maintained for reasons set forth therein.

Response to Applicants' Arguments on the New Matter Rejection

14) Applicants contend that they disclose polypeptides of SEQ ID NO: 3 which when used as immunogens elicit antibodies in animals that also recognize the native cytotoxic protein of *Helicobacter pylori*. Applicants state that they are not claiming that the native protein is non-cytotoxic, but that the polypeptides of the invention (useful as immunogens) are non-cytotoxic or have reduced cytotoxicity. Applicants submit that the claim includes the feature that the polypeptides of the invention are immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3, i.e., 'the same antibodies recognize the polypeptides as recognize the native protein having the amino acid of SEQ ID NO: 3' and that the polypeptides exhibit no toxicity or reduced cytotoxicity. Applicants submit that the specification at lines 21-30 of page 14 teaches the polypeptides of the invention which consist of at least 3-5 amino acids, and more preferably at least 8-10 amino acids, and even more preferably at least 11-15 amino acids, or which is immunologically identifiable with a polypeptide encoded in the [designated] sequence'. Applicants further state that the originally filed claims and the specification at page 4, lines 1-4 amended to include the language of the originally filed claim 8, specify that the polypeptides of the invention 'exhibit substantially no toxicity or substantially reduced toxicity'.

Applicants' arguments have been carefully considered, but are non-persuasive. Contrary to Applicants' contention, the polypeptides of the invention, which are useful as immunogens and which have 'no cytotoxicity' or 'reduced cytotoxicity', do not have descriptive support in the specification, as originally filed. A polypeptide having the amino acid sequence of SEQ ID NO: 3 which has cytotoxic activity and which causes vacuolation and death of a number of eukaryotic cell types has descriptive support in the instant specification, for example, at lines 31-39 on page 5 of the specification. The specification at lines 21-30 of page 14 describes a polypeptide which consists of at least 3-5 amino acids, and more preferably at least 8-10 amino acids, and even more preferably at least 11-15 amino acids, **or** a polypeptide which is immunologically identifiable with a polypeptide encoded in the sequence'. Nothing in this part of the specification associates the polypeptide or portions thereof with 'no cytotoxic activity or reduced cytotoxic activity'. The original claim 8 is not supportive of a recombinant polypeptide comprising at least fifteen, ten or five contiguous amino acids from the amino acid sequence of SEQ ID NO: 3, **and** having the two *required* functional properties of: (a) immunological identifiability by antibodies that react

specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 **and**, (b) no cytotoxic activity or reduced cytotoxic activity.

Response to Applicants' Arguments on Cover *et al.* ('132 and 1992)

15) I. The patent of Cover *et al.* ('132):

With regard to Cover *et al.* ('132), Applicants state that Cover *et al.* ('132) disclosed the purification of a cytotoxin of *Helicobacter pylori* with vacuolating activity. Applicants contend that at lines 7-9 of column 2, Cover *et al.* ('132) state that 'an' object of their invention is to provide a substantially pure antigenic composition with vacuolating toxin activity, and that one embodiment of the invention is a purified antigenic composition with vacuolating toxin activity. Applicants point to lines 37-39 in column 2 of Cover *et al.* ('132) and state that the CB antigen is defined as the 'functionally active non-denatured vacuolating toxin'. Applicants submit that Cover *et al.* ('132) do not teach or suggest the use of portions of the cytotoxin that exhibit substantially no, or substantially reduced cytotoxicity as claimed in the instant application. Applicants state that the Office's position that Cover's patent '132 teaches a 23 amino acid fragment of the CB antigen which comprises the antigenic polypeptide is incorrect, because the Patentees performed N-terminal sequencing of a purified toxin to deduce the amino acid composition and sequence of the N-terminus of the toxin. Applicants assert that this portion was not used as an immunogen, rather was performed to partially characterize the entire CB toxin. Applicants submit that Cover *et al.* ('132) (I) did not obtain and purify a 23 amino acid fragment from the toxin, and that such is neither the purpose nor the result of N-terminal sequencing. With this, Applicants conclude that Cover *et al.* ('132) (I) do not teach every element of the claims and does not anticipate the claims within the meaning of 35 U.S.C. § 102.

Applicants' arguments have been carefully considered, but are non-persuasive. Instant claims, as amended, do not include the limitations: 'substantially no cytotoxicity', or 'substantially reduced cytotoxicity'. Cover *et al.* ('132) do not have to teach the purified polypeptide or the purified polypeptide fragment, because the instant claims do not require the claimed polypeptide or the fragment to be purified. Cover *et al.* ('132) did not teach just one object of the invention, but taught more than one embodiment and several objects of their invention. One such embodiment is antigenic fragments of a purified CB antigen. Cover *et al.* ('132) expressly disclosed that the term CB antigen includes 'antigenic fragments of the holotoxin, whether derived from *H. pylori* or

synthetically or **recombinantly** produced' [Emphasis added]. Cover *et al.* ('132) expressly taught that their invention contemplates fragments of proteins having substantial homology to the CB antigen as well as CB antigen analogs (see lines 41-47 in column 2). Cover *et al.* ('132) taught a parenteral *H. pylori* vaccine that includes the fragments of the CB protein, which is administered with an adjuvant, or by itself in a suitable buffer (see lines 42-50 in column 16). Via Example 7, Cover *et al.* ('132) taught the isolated antigenic fragment of the CB protein, usable in ELISA, for detection of antibodies to *Helicobacter pylori*. This indicates that the prior art antigenic fragment is immunologically identifiable by antibodies specifically reactive with the native polypeptide. One such antigenic fragment is depicted as the 23 amino acid-long sequence at the top of Table 2 in columns 11 and 12. Cover's ('132) Sequence Listing in columns 17 and 18 depicts the structure of this 23 amino acid sequence construct as, Ala Phe Phe Thr The Val Ile Ile Pro Ala Ile Val Gly Gly Ile Ala Thr Gly Thr Ala Val Gly Thr, which is structurally identical to the polypeptide fragment located at positions 34-56 of the instantly recited amino acid sequence of SEQ ID NO: 3. Cover's ('132) 23 amino acid-long antigenic fragment is long enough to serve as an immunogen or antigen, irrespective of whether it is purified or not, since it is well known in the art that the smallest peptides which elicit antibodies that bind to the original full length protein are six amino acids in length. See the first sentence under 'Size of the Peptide' on page 76 of Harlow *et al.* Because of the 100% sequence or structural identity between the instantly recited fragment and the prior art protein fragment of 23 contiguous amino acids, the prior art protein fragment is viewed as structurally the same as the instantly claimed polypeptide fragment, and therefore is expected to have the same functional properties of the instantly claimed protein fragment. It should be noted that the recited 'fragment' in the claims, as amended, is not required to be immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3; and is not required to be of no cytotoxicity or reduced cytotoxicity. Only the recited polypeptide of SEQ ID NO: 3 is required to have the two functions or properties recited in parts (i) and (ii) of the instant claims.

II. The reference of Cover *et al.* (1992):

With regard to the teachings of Cover *et al.* (1992), Applicants state that Cover *et al.* (1992) teach the purification to homogeneity of a vacuolating cytotoxin from *Helicobacter pylori*, and that one step in evaluating the purified protein in Cover *et al.* (1992) was to perform N-terminal amino

acid sequencing to determine the amino acid sequence of the first 23 amino acids. Applicants submit that Cover *et al.* (1992) did not purify a fragment of the cytotoxin comprising 23 amino acids. Applicants state that amino acid sequencing breaks the peptide bond of the N-terminal amino acid and analyzes it, and subsequently the next amino acid is cleaved from the peptide chain. With this, Applicants conclude that Cover *et al.* (1992) does not include every limitation of the claims and does not anticipate the claims within the meaning of 35 U.S.C. § 102.

Applicants' arguments have been carefully considered, but are not persuasive. The reference of Cover *et al.* (1992) does not have to teach a purified 23 amino acid fragment of the cytotoxin, because none of the instant claims include the limitation 'purified', or require the claimed polypeptide or its fragment to be 'purified'. As set forth under the art rejection(s) below, Cover *et al.* (1992) do teach the claimed composition.

It is important to note that Cover's ('132 or 1992) 23 amino acid-long antigenic polypeptide fragment is not excluded from the scope of the claimed invention. In the instant application, it should be further noted that Applicants have never denied that Cover's ('132 or 1992) 23 amino acid-long polypeptide is not structurally the same as the polypeptide fragment located at positions 34-56 of the instantly recited amino acid sequence of SEQ ID NO: 3. In fact, all through the instant specification, Applicants have acknowledged Cover's ('1992) disclosure of this 23 amino acid polypeptide. This is *prima facie* evidence that this polypeptide fragment taught by Cover (1992) was already known in the art at the time of the invention. For example, in the first part of page 6 of the specification, Applicants cite the reference of Cover *et al.* (1992) and state that 'the previously described 87 kDa results from either the further processing of the 100 kDa protein or from proteolytic degradation of a larger protein during purification'. See also lines 27-30 on page 47 of the specification. Therefore, Cover's (1992) 87 kDa protein comprising the 23 amino acid-long amino terminal portion qualifies as a proteolytically degraded fragment. The fourth full paragraph on page 45 of the Applicants' specification acknowledges that the amino acid fragment encoded by the nucleotides 116-413 of the sequence shown in Figure 1 (i.e., SEQ ID NO: 2) and fused to a part of the MS2 polypeptide includes 'the 23 amino acids previously identified'. The instant specification at lines 10-14 of page 47 readily admits that this 23 amino acid-long sequence is identified as 'the amino terminus of the previously described 87 kDa vacuolating protein, ... J. Biol. Chem. 267: 10570-75 (1992)'. Therefore, what is claimed in the instant claims encompasses

the previously described Cover's (1992) 23 amino acid-long sequence of the 87 kDa polypeptide of *H. pylori,* including the completely neutralized polypeptide. See the art rejection below.

New Rejection(s)

Applicants are asked to note the new rejection(s) made below in this Office Action. The new rejections are necessitated by Applicants' amendments to the claims, and/or the base claims, wherein the phrase reciting the generic toxicity: 'substantially no toxicity, or substantially reduced toxicity' is replaced with the phrase: 'no cytotoxic activity or reduced cytotoxic activity'. The amendments to the claims change the scope of the claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

16) Claims 38 and 44-46 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 38 and 44-46 include the new limitations: exhibits 'no cytotoxic activity or reduced cytotoxic activity'. Accordingly, the claims are now drawn to an immunogenic composition comprising an immunologically effective amount of a polypeptide or recombinantly produced polypeptide comprising the amino acid sequence of SEQ ID NO: 3, or a fragment of the amino acid sequence of SEQ ID NO: 3, which polypeptide is *required* to have the *two* functional properties: (a) immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 *and,* (b) exhibition of no cytotoxic activity or reduced cytotoxic activity. Applicants appear to point to lines 21-30 of page 14 of the specification as providing descriptive support for the new limitations. However, this part of the specification, or the rest of the specification as originally filed, or the original claim 8, does not provide descriptive support for the newly added limitations: 'no cytotoxic activity or reduced cytotoxic activity', and/or for a polypeptide or a recombinantly produced polypeptide comprising the amino acid sequence of SEQ ID NO: 3, *and* having the two *required* functional properties of: (a) immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 *and,* (b) no cytotoxic activity or reduced cytotoxic activity. Instead, the paragraph bridging pages 5 and 6 of the specification, as originally filed, provides descriptive support for a *H. pylori* cytotoxin 'having cytotoxic activity' which 'cytotoxin causes vacuolation

and death of a number of eukaryotic cell types'. The original claim 8 is limited to a 'recombinant' protein whereas the polypeptide recited in claims 38 and 45 is not. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or point to specific pages and line numbers in the specification, as originally filed, where support for such recitations can be found.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

17) Claims 38 and 44-46 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 38 and 44-46 are vague and indefinite in the recitation: 'reduced cytotoxic activity', because it is unclear what degree of cytotoxicity is encompassed in this limitation. The term 'reduced' is a relative term which renders the claims indefinite. The term 'reduced cytotoxic activity' is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

Rejection(s) under 35 U.S.C. § 102

18) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
> **(e)(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

19) Claims 38 and 44-46 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (US 6,054,132, filed 02/26/1992 - already of record) (Cover *et al.*, '132) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

Instant claims encompass an immunogenic composition comprising an immunologically effective amount of a fragment of the amino acid sequence of SEQ ID NO: 3, with or without a pharmaceutically acceptable carrier. It is noted that the 'fragment' recited in the instant claims is not required to exhibit no cytotoxic activity or reduced cytotoxic activity and/or immunological identifiability by an antibody that reacts specifically with *H. pylori* cytotoxin. It is further noted that the transitional recitation 'comprising' is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* ('132) taught a parenteral *H. pylori* vaccine that includes the fragments derived from the CB protein, which is administered with an adjuvant, or by itself in a suitable buffer (see lines 42-50 in column 16). Cover *et al.* ('132) expressly taught antigenic fragments of a purified CB antigen. Cover *et al.* ('132) expressly disclosed that the term CB antigen includes 'antigenic fragments of the holotoxin, whether derived from *H. pylori* or synthetically or **recombinantly** produced' [Emphasis added]. Cover *et al.* ('132) expressly taught that their invention contemplates fragments of proteins having substantial homology to the CB antigen as well as CB antigen analogs (see lines 41-47 in column 2). Via Example 7, Cover *et al.* ('132) taught the antigenic fragment of the CB protein, usable in ELISA, for detection of antibodies to *Helicobacter pylori*. This indicates that the prior art antigenic fragment is immunologically identifiable by antibodies specifically reactive with the native polypeptide. One such antigenic fragment is depicted as the 23 amino acid-long sequence at the top of Table 2 in columns 11 and 12. Cover's (1992) Sequence Listing in columns 17 and 18 depicts the structure of this 23 amino acid sequence construct as, Ala Phe Phe Thr The Val Ile Ile Pro Ala Ile Val Gly Gly Ile Ala Thr Gly Thr Ala Val Gly Thr, which is structurally identical to the polypeptide fragment located at positions 34-56 of the instantly recited amino acid sequence of SEQ ID NO: 3. Cover's ('132) 23 amino acid-long antigenic fragment is long enough to be immunogenic, since it is well known in the art that the smallest peptides which elicit antibodies that bind to the original full length protein are six amino acids in length. See the first sentence under 'Size of the Peptide' on page 76 of Harlow *et al.* Because of the 100% sequence or structural identity between the instantly recited fragment and the prior art protein fragment of 23 contiguous amino acids, the prior art protein fragment is viewed as structurally the same as the instantly claimed polypeptide fragment, and therefore is expected to have the same functional properties of the instantly claimed protein fragment.

Claims 38 and 44-46 are anticipated by Cover *et al.* ('132). Harlow *et al.* is not used as a secondary reference in combination with Cover *et al.* ('132), but rather is used to show that every element of the claimed subject matter is disclosed by Cover *et al.* ('132) with the unrecited limitation(s) being inherent in view of what is known in the art as explained above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

20) Claims 38 and 44-46 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Cover *et al.* (*J. Biol. Chem.* 267: 10570-10575, 25 May 1992 - already of record) (Cover *et al.*, 1992) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual.* Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988).

Instant claims are not afforded the priority benefit to PCT applications, PCT/EP93/00472 filed 03/02/93 and PCT/EP93/00472 filed 03/02/93, or to the foreign priority application, FI 92A000052 filed 03/02/92, since these applications lack descriptive support for the newly added limitations: 'no cytotoxic activity or reduced cytotoxic activity', and/or for a polypeptide or recombinantly produced polypeptide comprising the amino acid sequence of SEQ ID NO: 3, having the two *required* functional properties of: (a) immunological identifiability by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO: 3 *and*, (b) no cytotoxic activity or reduced cytotoxic activity.

Instant claims are interpreted in this rejection as encompassing an immunogenic composition comprising an immunologically effective amount of a polypeptide comprising a fragment of the amino acid sequence of SEQ ID NO: 3, with or without a pharmaceutically acceptable carrier, wherein the polypeptide is required to exhibit no cytotoxic activity or reduced cytotoxic activity and immunological identifiability by an antibody that reacts specifically with *H. pylori* cytotoxin. It is noted that the transitional recitation 'comprising' is open-ended claim language and therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

Cover *et al.* (1992) taught the culture supernatants comprising an amount of *Helicobacter pylori* vacuolating toxin (i.e., polypeptide) having a molecular weight of 87,000 wherein the toxin's vacuolating activity is completely neutralized, i.e., rendered non-cytotoxic or less cytotoxic. The toxin is reactive with an antiserum raised against the purified *Helicobacter pylori* protein of a molecular weight of 87,000 (see paragraph bridging pages 10572 and 10573). That the prior art culture supernatants comprising the polypeptide are intrinsically immunogenic and/or serve as

immunogenic compositions is inherent from the teachings of Cover *et al.* (1992). It is important to note that Cover's (1992) *Helicobacter pylori* vacuolating toxin (i.e., polypeptide) having a molecular weight of 87,000, which was completely neutralized, comprises an amino terminal portion having the sequence, AFFTTVIIPAIVGGIATGTAVGT, which amino terminal sequence has 100% sequence identity with a 23 amino acid-long contiguous polypeptide fragment that stretches between positions 34-56 of the instantly recited SEQ ID NO: 3 (see the very first sequence depicted at the top portion of Cover's Table III). Because the prior art protein has the same molecular weight of 87,000 as the instantly claimed polypeptide, the 100% structural identity with an N-terminal portion of the instantly recited amino acid sequence of SEQ ID NO: 3, the immunological identifiability by an antiserum that reacts with the *Helicobacter pylori* vacuolating toxin of molecular weight 87,000, and the reduced or no cytotoxic activity, it is considered that there is sufficient overlap between the prior art *Helicobacter pylori* polypeptide and the instantly recited polypeptide of SEQ ID NO: 3 to conclude that Cover's (1992) culture supernatant comprising the protein, with its vacuolating toxin activity completely neutralized, anticipates the claimed composition. That the broth contained in the prior art culture supernatants serves as a pharmaceutically acceptable carrier at least for the immunization of animals is inherent from the teachings of Cover *et al.* (1992).

Furthermore, the term 'recombinantly produced' in claims 44 and 46 represent process limitations in product claims. The prior art polypeptide anticipates the instantly claimed polypeptide, irrespective of how it is obtained. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art polypeptide comprising the above-identified N-terminal fragment differs from that of the instantly

recited polypeptide of the amino acid sequence SEQ ID NO: 3 comprising the same structurally identical fragment.

Claims 38 and 44-46 are anticipated by Cover *et al.* (1992).

Remarks

21) Claims 38 and 44-46 stand rejected.

22) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

23) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (703) 872-9306.

24) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

25) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to

Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2004

SD
S. DEVI, PH.D.
PRIMARY EXAMINER